Remarks

Applicant has submitted new claims 18 and 19. The disclosure at page 5, lines 27-30 provide support for these claims. Support for the amendments to claims 8 and 11 can be found at the examples of the application.

As stated in the previous amendment, this invention is directed to effervescent compositions. Effervescent compositions are most often prepared using two dry ingredients that react in the presence of water to liberate CO_2 gas, usually via an acid-base interaction. A continuing problem with effervescent compositions is that the components usually employed to create the effervescence, a carbonate or bicarbonate and an edible organic acid (called the "effervescent couple"), can react before intended use by, for example, exposure to humidity, condensation, or other conditions that expose the effervescent couple to water. The resulting effervescent reaction forms a sodium salt of the edible organic acid (e.g., sodium citrate), CO_2, and water. Thus, once the degradation process begins, it can easily accelerate because of the water produced by the reaction.

Another problem with effervescent tablets is that certain medicines delivered via effervescent compositions can be vulnerable to degradation by one or both members of the effervescent couple or by the water liberated during the degradation of the effervescent couple. Aspirin is well known to be susceptible to degradation upon exposure to humid environments. These problems can be particularly acute in effervescent tablets, because the compression step usually associated with tablet formation forces the members of an effervescent couple and the medicine into very close

proximity. In humid environments and other damp conditions, the problems can become particularly acute.

Applicants have discovered that the stability of effervescent couples and, as a result, the medicine delivered with the effervescent couple, can be improved. Compositions in accordance with the invention are prepared by incorporating at least one member of the effervescent couple in a dispersion of a fusible sugar, sugar alcohol or sugar substitute. This dispersion is, however, more than a simple blending of powdered materials. As noted in the application, page 1, lines 35-37 and page 2, lines 12-15, stability is increased when one member of an effervescent couple is dispersed in a melted sugar, sugar alcohol or sugar substitute.

In the Office Action of November 17, 2009, the Examiner issued rejections to all the pending claims. The Examiner rejected all the claims under the written description requirement of Section 112, and rejected all the claims under Sections 102 and 103 in light of U.S. Patent No. 3,872,227 to Hoff ("Hoff"), GB Patent Application No. 3,307,857 to Leslie ("Leslie") and U.S. Patent No. 6,071,539 to Robinson et al. ("Robinson"), either alone or in various combinations.

The rejection of claims 8-17 based on the written description requirement is respectfully traversed. The Examiner has rightly pointed out that the list of pharmaceutical active substances on page 3, lines 5-35 does not use the words "degradable active substances" in *ipsis verbis*. Rather, the list describes many different active substances known for pharmaceutical use that may be used with the invention. It is fair to say that each of these different active compounds has a different "degradation

profile," in that they are each susceptible to degradation by humid, acidic and basic environments to differing degrees. Some may be highly resistant to acidic environments but vulnerable to basic environments, while others may have the opposite profile or even an orthogonal profile.

The Examiner is nevertheless directed to page 1, lines 35-37 of the application, where the inventors say, "It has now been found, surprisingly, that the stability of medicament-containing effervescent preparations can be increased by a process in which a preparation component is melted." The Examiner is further directed to page 9, line 26 - page 10, line 2, where aspirin preparations made in accordance with the invention were compared to conventional technology, and the conversion of aspirin (acetylsalicylic acid) into salicylic acid, the "degradation product" of aspirin was measured. Although this disclosure is not *ipsis verbis*, it shows that the inventors possessed the claimed invention at the time of the invention. (For claims 16 and 17, the example actually is *ipsis verbis*.)

The Examiner's position that the term "degradable pharmaceutically active substances" should expressly be set forth must be reconsidered in light of the recent case of Ariad v. Lilly, Case No. 2008-1248, Slip Opinion, (Federal Circuit March 22, 2010, en banc). The Federal Circuit concluded that one of the "few broad principles" guiding a written description analysis is that "the description requirement does not demand . . . that the specification recite the claimed invention in haec verba . . . ." (Slip op. at 25.) So, *haec verba* or *ipsis verbis* is not required. Rather, the aspirin example on page 9 shows one skilled in the art that the structure and technique described in the specification stabilizes a degradable pharmaceutically active substance. The reason the structure and technique works is that the effervescent couple is stabilized (see p. 1, lines 7 – 33) which in turn

stabilizes the active ingredient (see p. 9, line 26 – p. 10, line 2). This structure and technique are disclosed to work with the compounds listed on page 3, which are more or less vulnerable to degradation by the same aspirin pathway. Thus, the inventors possessed the use of the inventive structure and composition with aspirin, with degradable pharmaceutically active substances, and with all the compounds listed on page 3.

The Examiner's rejections of claim 8 under Section 102 and 103 in light of Hoff are also respectfully traversed. The Examiner relies on Example 7 of Hoff and claims that the structure resulting from moistening in a kneader with an alcoholic solution and subsequent drying in a fluidized bed is substantially identical to the structure of claim 8, formed by melting, dispersing, and resolidifying. The Examiner relies on M.P.E.P. 2113 to shift the burden of going forward. The Examiner argues that the structures are substantially identical because both products are "tablets" and both have an effervescent couple and a sugar substitute.

The structure of Example 7 of Hoff, however, is not substantially identical to the structure of claim 8. M.P.E.P 2113 requires more than a superficial resemblance. The fact patterns pointed out in M.P.E.P 2113 require much closer identity than found in Hoff.

The product by process claim of *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985) was rejected where the only process difference between the claimed product and the prior art was the addition of metal oxide and carboxylic acid as separate ingredients instead of the addition of a pre-reacted metal carboxylate. Both the prior art

product and the claimed product contained a metal carboxylate. The M.P.E.P. reports that a metal carboxylate produced in-situ does not change the end product. Thus, the cited art and the product by process of *Thorpe* were identical.

A product by process claim to a zeolite was rejected by *In re Marosi*, 710 F.2d 798, 802, 218 USPQ 289, 292 (Fed. Cir. 1983) because the claimed zeolite was manufactured by mixing together various inorganic materials in solution and heating the resultant gel to form a crystalline metal silicate claimed to be essentially free of alkali metal. The prior art described a process of making a zeolite that removed alkali metals by ion exchange. Again, the claimed zeolite and the prior art zeolite were identical because the only difference was reportedly between alkali metals that had been removed and alkali metals that had not been present in the first place.

Likewise, *Ex parte Gray*, 10 USPQ2d 1922 (Bd. Pat. App. & Inter. 1989) said that genetically engineered human nerve growth factor (b-NGF) did not distinguish from the *same* factor that had been isolated from human placental tissue.

These situations are easily distinguished from Hoff. The differences between the claimed structure and Hoff "would be expected to impart distinctive structural characteristics to the final product." M.P.E.P 2113 (citing, *In re Garnero*, 412 F.2d 276, 279, 162 USPQ 221, 223 (CCPA 1979)). In Hoff, the reported "moistening" of the effervescent couple, followed by drying in a fluidized bed serves only to clump the materials together, which would leave large numbers of effervescent crystals exposed on the surface of the resulting granules, like sprinkles on an ice cream cone. The claimed structure, on the other hand, requires the sugar to be melted, thereby losing its crystalline

orientation. The effervescent material is then dispersed in the sugar, so the sugar surrounds the effervescent material (either powder specks in the case of a suspension or individual molecules in the case of a solution) and the sugar is resolidified to form a matrix (see page 6, lines 1-5 of the application). The resulting structure would be expected to look like chocolate chip ice cream. The occasional chocolate chip might be exposed, but most chips are entirely enrobed in ice cream.

The Examiner's attention is also directed to claims 18 and 19, which expressly claim a product and process without water or a volatile solvent. These claims further distinguish over Hoff by excluding the solvent used to "moisten" the powder. Support for these claims is found at page 5, lines 27-30 of the application.

The Examiner rejected claim 8 over Leslie, even though the rejections of claims 9, 10, 12, and 13 were withdrawn because sodium saccharin melts above 200° C. The melting point of sodium saccharin is also significant because the sodium saccharin in Example 3 of Leslie *does not melt*. Thus, the material in Example 3 that the Examiner identifies as a sugar substitute as defined by claim 8 *did not melt*. As a result, the structure formed in Example 3 is not formed by "melting said ingredient and dispersing said at least one of said CO_2 donor and said acidic component therein and resolidifying said ingredient," because the "ingredient" did not melt, and so nothing could be dispersed in the melted ingredient, and there was no ingredient to resolidify. This is not a matter of opinion; it is a matter of physics. As discussed above, the claimed structure is like chocolate chip ice cream. The structure disclosed in Leslie is like chocolate chips and ice cream pellets floating separately in gelatin. Since the structures are not the same, Leslie does not teach or suggest the composition of claim 8. It is not applicant's burden to

provide additional evidence showing the difference in structure. There is a sound basis for asserting that the claimed structure is fundamentally different from Hoff and Leslie based on the fact that the claimed sugar melts, while the Hoff and Leslie materials do not melt. Thus, the Examiner's speculative argument that the structures may be the same does not establish a prima facie case to shift the burden under M.P.E.P 2113.

The Examiner also rejected the composition and process claims in view of Robinson. The Examiner argued that claims 8-10 were anticipated by Robinson because that patent teaches effervescent granules and hot-melt extrudable binders forming a eutectic mixture (solid solution) with the acidic agent and active agents. The Examiner also rejected claims the process claims as obvious over Robinson.

Claims 8 and 11 have been amended to clarify that the degradable pharmaceutical active in not incorporated into the melted material, as was done in Table 4 of Robinson. The claims have also been amended in light of the examples to require that the ingredient comprise at least 30% by weight of the blend formed when the ingredient is melted.

Robinson is not concerned with the long term stability of the active ingredient. Robinson only cares about the stability of the active ingredient during the extrusion process. The claimed invention does not put the active ingredient though an extrusion process. This difference means that Robinson may use far less xylitol (in the examples that use xylitol) because Robinson need only protect the active ingredient for the "extremely short exposure times of compounds to elevated temperatures" (Col. 3, l. 16-18). Tablets made in accordance with Robinson are prepared by first drying the materials at 40° C. overnight, preferably in a vacuum, then mixing the effervescent materials and

the binder. This mixture is then hot-melt extruded as part of the process for making granules comprising the effervescent couple and the binder (Example 1). These granules are then formulated into effervescent compositions (Example 3 and Table 3) by mixing with other ingredients or made into tablets using conventional techniques. In contrast to the remarks section of the previous amendment, Table 4 of Robinson reports mixtures of materials that, according to Example 5, may or may not be extruded.

As reported in the previous amendment, an analysis of the examples containing xylitol in Robinson shows that none of the examples rises to the same weight percentage as the examples tested in the present application. In the application, the lowest weight percentage blend had a weight percentage of 30% xylitol (example 3), while the highest weight percent in a Robinson extruded granule is about 15%, as shown in the table below.

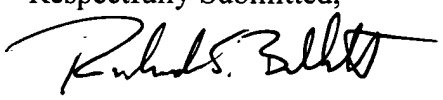
Weight Percentages of Effervescent Granules in Robinson			
Example	Wt. % Acid	Wt. % Base	Wt. % Binder
J	34	51	15
K	40	50	10
M	35	35	10
N	37	38	8
O	40	40	10
P	40	40	3.5
Q	35	35	13.5
R	37	38	11.5
S	40	40	13.5

The formulations reported in Robinson's of Table 4 cannot be used to determine the blend weight percentages because the amount of the mannitol or xylitol that is put through the hot melt extrusion process is not defined.

The Robinson process cannot teach or suggest the process claims, for the same reasons that is cannot teach or suggest the product claims.

The claimed invention is not taught or suggested by the cited references, either alone or in combination. Hoff and Leslie are taste masking patents. Robinson is directed to controlling the rate of effervescence. Combining these patents would present insurmountable difficulties because nothing in Hoff and Leslie is melted, except, perhaps, for propylene glycol, which is not within the scope of the invention. Applicant has developed a unique structure and process for creating that unique structure. Applicant respectfully requests withdrawal of the rejections and allowance of the claims.

Respectfully Submitted,



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